

Support for amended claim 1 and new Claims 47-59 may be found throughout the specification. Particularly, support for amended Claim 1 may be found, for example, at page 3, lines 13-23 wherein it is stated that the present invention is directed to a targeted therapeutic delivery system for the controlled delivery of a therapeutic compound to a region of a patient comprising, in combination with a therapeutic compound, stabilized lipid microspheres encapsulating a gas or gaseous precursor and an oil.

Support for Claim 47 may be found, for example, at page 60, line 13 through page 69, line 11 wherein it is stated that the gas or gaseous precursor of the targeted therapeutic delivery system may be fluorine, perfluorocarbons, sulfur hexafluoride, and perfluoroethers.

Support for Claims 48-50 may be found, for example, at page 36, line 11 through page 39, line 3 wherein various exemplary lipids for use in the present invention are set out.

Support for Claims 51-55 may be found, for example, at page 9, line 15 through page 23, line 7 wherein it is stated that the oil may be silicone oil, cod liver oil, mineral oil, plant oil, oil comprising fluorinated triglycerides, biocompatible saturated fatty acids, biocompatible unsaturated fatty acids, and biocompatible partially hydrogenated fatty acids, silicon-based oils, and synthetic oils. In addition, various plant oils, silicon-based oils and synthetic oils are set out.

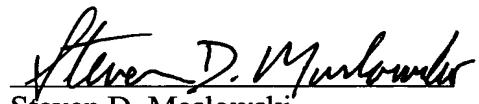
Support for Claims 56 and 57 may be found, for example, at page 46, lines 6-8 wherein it is stated that the therapeutic compound may be attached to the targeted therapeutic delivery system such that it is incorporated into the void of the microsphere or onto the inner or outer microsphere surface.

Support for Claim 58 may be found, for example, at page 15, line 20 through page 16, line 24 wherein it is disclosed that the targeted therapeutic delivery system may further comprise a targeting ligand.

Support for Claim 59 may be found, for example, at page 19, lines 15-22 wherein it is stated that the oils and waxes may be used to dissolve the therapeutic compound.

The claims are fully supported in the Application as originally filed and no new matter is added. We respectfully request prompt allowance of the claims.

Respectfully submitted,


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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please cancel Claims 2 through 24 without prejudice. Please amend Claim 1 as follows:

1. (Amended) A targeted therapeutic delivery system for the controlled delivery of a therapeutic compound to a region of a patient comprising, in combination with a therapeutic compound, stabilized lipid microspheres encapsulating a gas or gaseous precursor [filled microsphere wherein said gas or gaseous precursor filled microsphere comprises] and an oil[, a surfactant, and a therapeutic compound].

Please add new Claims 47-59 as follows:

47. (New) The targeted therapeutic delivery system of claim 1 wherein said gas or gaseous precursor is selected from the group consisting of fluorine, perfluorocarbons, sulfur hexafluoride, and perfluoroethers.

48. (New) The targeted therapeutic delivery system of claim 1 wherein said lipid is selected from the group consisting of fatty acids; lysolipids; phosphatidylcholines; phosphatidylethanolamines; phosphatidylserine; phosphatidylglycerol; phosphatidylinositol; sphingolipids; sphingomyelin; glycolipids; ganglioside GM1; ganglioside GM2; glucolipids; sulfatides; glycosphingolipids; phosphatidic acids; lipids bearing sulfonated mono-, di-, oligo- or polysaccharides; lipids with ether and ester-linked fatty acids; polymerized lipids; cardiolipin; phospholipids with short chain fatty acids of 6-8 carbons in length; synthetic phospholipids with

asymmetric acyl chains; 6-(5-cholest-3 β -yloxy)-1-thio- β -D-galactopyranoside;

digalactosyldiglyceride; and lipids bearing a covalently bound polymer.

49. (New) The targeted therapeutic delivery system of claim 1 wherein said lipid comprises at least one phosphatidylcholine, at least one phosphatidylethanolamine, and at least one phosphatidic acid.

50. (New) The targeted therapeutic delivery system of claim 49 wherein said phosphatidylcholine is selected from the group consisting of dioleoylphosphatidylcholine, dimyristoylphosphatidylcholine, dipalmitoylphosphatidylcholine, and distearoylphosphatidylcholine; said phosphatidylethanolamine is selected from the group consisting of dipalmitoylphosphatidylethanolamine, dipalmitoylphosphatidylethanolamine-PEG 5,000, dioleoyl-phosphatidylethanolamine, and N-succinyl-dioleoyl-phosphatidylethanolamine; and said phosphatidic acid is dipalmitoylphosphatidic acid.

51. (New) The targeted therapeutic delivery system of claim 1 wherein said oil is selected from the group consisting of silicone oil, cod liver oil, mineral oil, plant oil, oil comprising fluorinated triglycerides, biocompatible saturated fatty acids, biocompatible unsaturated fatty acids, biocompatible partially hydrogenated fatty acids, silicon-based oils, and synthetic oils.

52. (New) The targeted therapeutic delivery system of claim 51 wherein said plant oil is selected from the group consisting of peanut oil, canola oil, olive oil, safflower oil, corn oil, and mazola oil.

53. (New) The targeted therapeutic delivery system of claim 51 wherein said silicon-based oil is selected from the group consisting of vinyl-terminated fluids, hydride terminated fluids, silanol terminated fluids, amino terminated fluids, epoxy terminated fluids, carbinol terminated fluids, mercapto-modified silicon fluid, saturated silicon oil, unsaturated silicon oil, and aryl-alkyl substituted silicon oil.

54. (New) The targeted therapeutic delivery system of claim 51 wherein said synthetic oil is selected from the group consisting of saturated chains of C₁₂ to C₂₄ fatty acids and unsaturated chains of C₁₂ to C₂₄ fatty acids.

55. (New) The targeted therapeutic delivery system of claim 51 wherein said synthetic oil is selected from the group consisting of triolein, trimyristin, triacetin, tripalmitin, tristearin, tributyrin, glyceryl monoctanoate, and glyceryl monostearate.

56. (New) The targeted therapeutic delivery system of claim 1 wherein said therapeutic compound is attached to the surface of said microspheres.

57. (New) The targeted therapeutic delivery system of claim 1 wherein said therapeutic compound is encapsulated in said microspheres.

58. (New) The targeted therapeutic delivery system of claim 1 further comprising a targeting ligand.

59. (New) The targeted therapeutic delivery system of claim 1 wherein said therapeutic compound is dissolved in said oil.